

ABSTRACT

Charles University in Prague, Faculty of Pharmacy in Hradec Králové

Tutor – specialist: PharmDr. Jan Zitko, Ph.D.

Candidate: Ondřej Valášek

Title of diploma thesis: Pyrazine Derivatives as Potential drugs IV.

Even in the year 2016, tuberculosis is still worldwide problem which is addressed by many national and supra-national organizations trying to eliminate it. It burdens the most developing countries which don't usually have the opportunity to access the potential of modern medicine to its full extent. In relation to ineffective treatment, there grows prevalence of tuberculosis, which can't be managed by standard treatment. There is an urgent need to find new compounds and change structures of current antituberculars, which will help us defeat multi-drug resistant *M. tuberculosis*.

The objective of my work was to find out the influence of inversion of the amidic group in derivatives of pyrazin-2-carboxylic acid (-CO-NH- to -NH-CO-) and their efficacy and toxicity.

In the theoretical part I focused on resuming all the basic facts about tuberculosis and its causing agent, about possibilities in prevention and diagnostics as well as the antituberculars, both used and currently tested, which can help us in the future.

In the experimental part I wrote down the reactions and procedures, which were used to prepare seventeen derivatives of *N*-(5-chloropyrazin-2-yl)benzamides and two derivatives of *N*-(pyrazin-2-yl)benzamides, which were prepared from either reaction of benzoylchlorides with amines, or, in one case, by coupling reaction of substituted benzoic acid with amine in presence of *N,N'*-carbonyldiimidazole. New compounds were characterized by their melting points, elemental analysis, NMR and IR spectra.

Afterwards, each compound had its *in vitro* antimycobacterial, antibacterial and antifungal efficacy tested. Those compounds, that showed promising antimycobacterial efficacy, were subjected to *in vitro* cytotoxicity tests. Overall, there weren't many active new structures except for four molecules which were efficacious on *M. tuberculosis* and one efficient antibacterial compound.